Appendix A
Evidence Table

Summary Evidence Tables for Evaluating Effectiveness of Zevalin® and Bexxar®

Author/Year	Objectives	Study Design	Major Inclusion Criteria	Major Exclusion Criteria	Key Baseline Characteristic
Witzig/2002, Corresponding to FDA Study 106-04	To compare the efficacy of Zevalin® therapy in relapsed or refractory, low-grade or follicular NHL with that of Rituxan monotherapy.	Randomized controlled trial with masking of the primary endpoint for the review committee. 73 subjects assigned to Zevalin® and 70 to Rituxan, enrolled from 27 centers.	(1) Histologically confirmed, relapsed or refractory low-grade or follicular NHL or transformed from low-grade to intermediate-grade histology, requiring treatment due to increased tumor size, symptoms and/or symptomatic masses. (2) At least 18 years old. (3) Expected survival at least 3 months. (4) CD20+ antigen expression.	The following prior therapies: Myeloablation with autologous bone marrow transplantation or peripheral blood stem cell (PBSC) rescue; Radioimmunotherapy; Anti-CD20 therapy, including IDEC-Y2B8 and Rituxan; External beam radiation therapy; or G-CSF or GM-CSF within past 2 weeks.	Zevalin® n=73 / Ritux n= <65 48 / 4 65-75 17 / 2 >75 8 Follicular 55 / 58 Non-follic. 9 Transform. 9 Stage I/II 8 Stage III/ IV 65 / 6
FDA and IDEC Briefing Materials, Corresponding to FDA Study 106-06	(1) Determine the efficacy of Zevalin® therapy in relapsed or refractory follicular NHL subjects whose disease was refractory to previous treatment with Rituxan. (2) Determine the overall response rate (ORR) to Zevalin® therapy in follicular NHL patients.	Open-label, single-arm, 17-center study with 57 subjects, 54 of whom with follicular NHL.	Follicular NHL subjects who were previously treated with Rituxan 375 mg/m^2 times four and whose most recent treatment did not result in a partial response (PR) or complete response (CR), as documented by baseline and post-treatment CT scans and who now have disease progression, or who had progression of disease within 6 months of first Rituxan infusion (could have been in Rituxan arm of 106-04, without PR or CR, and needing therapy).	Similar to Witzig/106-04 above.	Mean age 54.4 (34-73 51% F, 49% M 7% Stage I/II, 90% St III/IV and 3% Unkno 54 follicular NHL subjects, 2 non-follicular NHL subjects and 1 transformed NHL subject.
Wiseman/2002	Assess the efficacy of Zevalin® in mildly thrombocytopenic patients with advanced relapsed or refractory low-grade, follicular or transformed NHL.	Phase II open-label, single-arm, 12-center study with 30 subjects.	Similar entry profile to Witzig/106-04 above, and requiring platelet count between 100-149.	Similar to Witzig/106-04 above.	Median age 61 (29-85 40% F, 60% M 2 small lymphocytic lymphomas, 25 follicu lymphomas and 3 transformed lymphom
Kaminski/2001	1) To establish the efficacy and safety of a single course of Bexxar® in patients meeting a strict chem.-refractory definition 2) to compare efficacy outcomes of the last chemo regimen wit the efficacy outcomes after Bexxar®.	Phase 3, nonblinded, single Bexxar® dose, multicenter study using an "internal control" (i.e., each patient served as their own control using a paired analysis). 60 subjects were studied. Primary endpoint: number of subjects with a	Adults with low-grade or transformed low-grade CD20-positive B-cell lymphoma who received at least 2 prior protocol-specified chemo regimens and did not respond or had a relapse within 6 months of completion of the last regimen.	Exposure to unlabeled or radiolabeled monoclonal antibodies (i.e., Rituxan®- naïve).	Median age 60 (38-82 63% male 60% Low-grade 38% transformed low grade 2% intermediate grad mantle cell Median duration of

		longer duration of response (defined as >30 days difference) after chemo regimen v. after Bexxar®. Assessment performed by a masked panel comprised of 2 independent teams consisting of 1 radiologist and 1 oncologist.	90 subjects entered the study.		response to last chem 3.4 months (1.7-6.9)